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10/591,817	09/06/2006	Makoto Taketo	2006_1487A	3081

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EXAMINER	
YAO, LEI	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,817	TAKETO ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-9,14,17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13 and 15-16,18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/6/2006, 11/27/2006, 11/27/2007, 12/24/2007, 12/2/2008, 9/2/2009*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group II (claims 10-13) with species intestine cancer and antibody to CXCR3 in the reply filed on 9/2/2009 is acknowledged.

Claims 15-19 are added.

Claims 1-19 are pending.

Applicant includes newly added claim 17 for examination in the response to restriction requirement (page 5). This has been considered, but not found persuasive because claim 17 is further drawn to an antibody against CXCR ligand of claim 16. Applicant has elected an antibody to CXCR3 self, not to its ligand for examination. Therefore claim 17 is currently withdrawn from consideration.

Claims 1-9, 14, 17 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention (claims 1-9 and 14) and non elected species (claim 17 and 19) there being no allowable generic or linking claim.

After reconsideration of the elected species in light of the prior art, the species of breast and melanoma cancers are rejoined to the species of intestine cancer (claim 12) for examination at this time.

Claims 10-13, 15-16, and 18, drawn to a method of treating cancer and/or preventing metastasis to the extent of intestine, breast and melanoma cancers comprising administering a composition comprising CXCR3 inhibitor (elect antibody), are examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 9/6/2006, 11/27/2006, 11/27/2007, 12/24/2007, 12/2/2008, 9/2/2009 are/is considered by the examiner and initialed copies/copy of the PTO-1449 are/is enclosed.

Claim Objection

Claims 10-13, 15-16, and 18, are objected to for reciting ...CXCR3 inhibitor according to claim 1". Claim 1 is not currently examined because it is drawn to non-elected invention. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

Claims 10, 13, 15-16 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating or preventing lymph node metastasis of CXCR3 expressing cancers comprising intestine cancer, breast and melanoma cancers comprising administrating anti-CXCR3 antagonist antibody, does not reasonably provide enablement for the full scope of the claims drawn

to treating a cancer or preventing metastasis of any cancer that includes the cancer cells not expressing the CXCR3 protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are broadly drawn to a method for treating a cancer or preventing metastasis comprising administrating CXCR3 inhibitor comprising anti-CXCR3 antagonist antibody.

To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provides an enabling disclosure of how to make and use a claimed invention. The objective of the claims is treating a cancer or preventing metastasis of a cancer with an inhibitory antibody to CXCR3. Thus, it would be expected that one of skill in the art would be able to treat any cancer or prevent metastasis of any cancer with an antagonist anti-CXCR3 antibody by inhibiting the signaling through CXCR3 without undue a quantity of experimentations.

The specification teaches that cancers expressing CXCR3 include melanoma, breast, intestine and ovary cancers (page 5, line 23-27) and teach the instant method is for treating or preventing metastasis of a cancer comprising administering CXCR3 inhibitor, wherein the cancers express CXCR3 (page 5, (2)-(3) and page 6, (10)-(12)). The specification teaches that CXCR3 is implicated in survival and metastasis of cancer and reduced CXCR3 expression has decreased metastatic frequency of the cell to lymph notes, while elevation of the expression of CXCR3 ligands, CXCL9 or CXCL10 in lymph nodes increases the metastatic cancer cell in the nodes. Such increasing reaction was suppressed by antibody to the ligands (page 9, line 9+). The specification provides working examples 1 and 2 showing correlation between CXCR3 expression and melanoma and colon cancer cells metastasis to lymph nodes (page 26 and 42). The specification specifically teaches that CXCR3 does not affect metastasis to lung and liver. Thus, in this application, the inventor established the relationship between the metastatic cancer cells and CXCR3 expression on those cells.

One cannot extrapolate the teachings of the specification to the scope of the claims because no teaching or direction/guideline is provided for the method of treating any cancer comprising those do not express CXCR3 on the cancer cells by a CXCR3 inhibitor through the CXCR3 signaling.

The state of the art has revealed such correlation, however, recognized that not all the cancer including some metastatic cancer cells express such protein as compared to the same normal cell type. Golz et al (WO2005103722) teach diagnostic and therapeutic for a disease including cancer associated with CXCR3 expression and list

numbers of cancer cells that do not differentially express the CXCR3. For example, the levels of CXCR3 in the normal thyroid is 18, while only 7 for the thyroid tumor (page 66, line 4-5 from bottom); Normal Lung expresses the protein at level 25 and lung tumor is about the same at 21 (page 68, line 19-20).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not provide objective evidence, guideline/direction for claimed method of treating any cancer or preventing metastasis of any cancer having no CXCR3 with an inhibitor of the CXCR3. Such treatment and prevention would is predictably not working based on the teaching of the specification and the records of the art.

Thus, in view of the teaching of the art and the specification, the nature of the invention and the breadth of the claims, one skill in the art could not practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-12, 15, 16 and 18 are rejected under 35 U.S.C. 102 (b) as being anticipated by Burns et al (Pub No. US 20030124628, pub date, July 3, 2003).

Claims are drawn to a method for treating cancer or preventing metastasis of cancer, which comprises administering the composition of CXCR3 inhibitor;
wherein the inhibitor is an antagonist antibody that inhibits signaling of CXCR3;
wherein the cancer is metastatic colon cancer (intestine).

Burns et al disclose a method of treating and preventing metastatic cancer comprising administering a patient an antagonist antibody of CXCR3 (paragraph 030, 032, 116, 182-188 and page 27). Burns et al disclose that the antagonist antibody is used for treating the cancers that are screened for expressing CXCR3 (paragraph 093-94) including colon, breast, and skin (melanoma) cancers cells that expresses CXCR3 on the surface [093, 112, 208]. Burns et al disclose that the antibody is selectively modulating the intracellular signaling triggered by ligand binding which is inhibited by anti-CXCR3 antibody (paragraph 021).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquires set forth in Graham V. john Deere Co., 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 25 U.S. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or obviousness.

1. Claims 10-13, 15, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burns et al (Pub No. US20030124628, pub date. July 3, 2003), in view of Blake Cady (Arch Surg, vol 119, page 1067-1072. 1984).

The claims are set forth above. Claim 13 is further drawn to the method, wherein the metastasis to lymph node.

The teachings of Burns et al are set forth above.

Burns et al do not teach the lymph node metastasis of those cancer cells.

Blake Cady teaches that the breast, melanoma, colon etc cancer are often metastasized to lymph node, which is an indication of metastasis of a cancer and teahes that removing the lymph node is not governor of a treatment for the cancers (abstract, line 12+ and page 1068-9).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the methods to treat breast, colon, and melanoma with anti-CXCR3 antibody with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated with expectation of success to combine the teaching of Burns et al with the teaching of B. Cady et al in order to benefit the treatment of the breast, colon, and melanoma cancer and preventing the lymph node metastasis of the cancers with CXCR3 antibody because Cady has suggested removal of the lymph nodes does not govern the survival of the patients and Burns et al teach the method of treating those cancers with an inhibitor that is anti-CXCR3 antibody. Therefore, the references in combination teach

every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (a)-(d) as follows:

Applicant's claims to an earlier effective filing date through Japan application NO 2004-065612 filed on 3/9/04 are acknowledged. Upon review of documents submitted to the Office, no English translation for the foreign priority document was provided with this application. Since intervening reference is applied below, the claims are currently given the priority date as the date of filing PCT application March 9, 2005.

2. Claims 10-13, 15, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable Robledo et al (JBC vol 276, page 45098-105, 2001) or Kawada et al (Cancer Res. Vol 64, page 4010-17, 2004, provided in the restriction requirement, 6/2009), or Goldberg-Bittman et al (Immu let, vol 93, page 171-178, March, 29, 2004) in view of Levanon et al (US 20050152906, priority to June 2003).

The claims are set forth above.

Robledo et al teach that CXCR3 is expressed in lymph node metastasized melanoma cells (figure 1-2), teach that the ligand of CXCR3 (Mig, CXCL9) trigger such chemotaxis (invasion) of melanoma cell to the lymph node (figure 5) and suggest that

interaction of signaling of CXCR3 and its ligand play a role during the tumor cell invasion and growth (page 45099, col 1, line 3).

Kawada et al also teach that high levels of CXCR3 is in lymph node metastasized melanoma cancer cells (figure 1), teach that the ligands of CXCR3 (CXCL9, 10, and 11) trigger such migration and invasion of the melanoma cells (page 4012, col1). Kawada et al teach that inhibition of expression of the CXCR3 by its antisense suppressed such metastasis (figure 4). Kawada et al further suggest that inhibition of CXCR3 receptor may be a potential therapeutic target of metastasis of melanoma and other CXCR3 expressing tumor cells (page 4016, col 2, last line).

Goldberg-Bittman et al teach breast adenocarcinoma expressing high levels of CXCR3 protein on the surface of the cells (figure 1 and 2) and the ligands of CXCR3 play an important role in the malignant process of the cells (figure 4 and page 176, col 2).

Although each of the reference has identified metastasis cell expressing CXCR3 and signaling of the ligand interaction plays a role in the cancer migration and invasion. none of the references did in vivo study of treating an animal with such cancers with an inhibitor of CXCR3 protein for signaling.

Levanon et al teach neutralizing antibodies functioned for inhibiting the signaling of the proteins having tyrosine sulfation sites and teach the protein including the chemokine receptor, CXCR3. Levanon et al specifically teach that the antibody could be use for treating a disease associated with the protein expression, for example, inhibiting of metastasis in animal model (paragraph 136, 168).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the methods to treat breast, colon, and melanoma with an inhibitor of CXCR3. One of ordinary skill in the art at the time the invention was made would have been motivated to combine the teaching of Burns et al with the teaching of Cady et al in order to benefit the treatment of cancer or preventing the metastasis of the cancer comprising metastasis to lymph nodes with an inhibitor of CXCR3 because Cady has suggested removal of the lymph nodes does not govern the survival of the patients and Burns et al teach the method of treating those cancers with antagonist antibody to CXCR3. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings to treat melanoma, breast, or colon cancer or prevent metastasis of the cancers with the antibody to CXCR3 because Lvanon et al have shown the antibody and method of using the antibody for treating a cancer. Therefore, the references in combination teach every limitation of the claims and the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao/
Examiner, Art Unit 1642

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643